Tissue levels of mercury in autopsy specimens of liver and kidney

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Fifty-one autopsy specimens of liver were analysed for total mercury. Thirteen specimens contained less than 10 mg/kg of mercury, with a minimum value of 1.4 mg/kg, indicating that death in suspected cases was not always due to lethal exposure to methylmercury. The methylmercury concentration in 28 livers was 10-30 mg/kg. Limited additional estimations have shown that 71% of the liver mercury was organic and that the level of mercury in the liver of a 7-month-old fetus was only 25% of that in the liver of the mother. In a patient who died in hospital with a blood mercury level of 4.1 µg/ml, the liver contained 16.5 mg/kg of mercury.

Differences between these results and those found in the outbreak of methylmercury poisoning in Japan are discussed. Any extrapolation of tissue mercury levels in relation to the toxic effects of methylmercury must take account of the intensity and duration of exposure.

The dominant signs of methylmercury poisoning are the consequence of damage to the nervous system and, in agreement with this, in autopsy material from victims of chronic methylmercury poisoning the obvious change is limited to the central nervous system.[1,2] Consequently it would have been important to estimate mercury concentrations in the different parts of the central nervous system in the victims poisoned by the consumption of bread contaminated by methylmercury and to relate the concentration to the clinical history of the victim. Unfortunately circumstances limited the analytical work to estimations of mercury in the livers of fatal cases, for which, with one exception, there was no clinical history. In some of the Minamata victims the liver was also included in the analysis for mercury[3,4] and a comparison of the liver contents of mercury in the two outbreaks is of interest.

METHOD

Altogether, 51 liver samples were analysed; 50 were sent in ethanol either by the police or by hospitals and one sample was taken by biopsy technique immediately after the death of a female patient who had been under clinical observation for a considerable time. Table 1 shows the sex and age distribution of the cases for which these data were available. In addition, estimation of mercury in kidneys was carried out on 2 cases and on the liver of a fetus approximately 7 months old.

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TABLE 1. SEX AND AGE DISTRIBUTION OF THE AUTOPSY CASES

Sex	Age in years				Age unknown	Total
	-10	11-20	21-50	51+		
Male	5	4	-	2	2	13
Female	13	6	14	-	5	38
Total	18	10	14	2	7	51

Liver samples, taken under the dehydrated layer, were homogenized in 0.9% saline. Homogenates were analysed for total mercury and in some cases for inorganic mercury by the method of Magos.[5] The liver sample taken by the biopsy method was analysed by both the method of Magos[5] and that of Magos & Clarkson.[6] Results are expressed in mg/kg wet weight. Kidney samples were treated and analysed similarly, but as even the innermost part of the samples showed signs of dehydration, making homogenization difficult and the results related to weight unreliable, this type of estimation was used in only 2 cases.

RESULTS

The results of the analysis of the 51 liver specimens are shown in Fig. 1. The geometric mean of the 51 results was 16.3 mg/kg (standard deviation 7.6-13.05). The lowest value was 1.4 mg/kg, found in a 10-year-old boy whose autopsy specimens were sent by the police. The mercury concentration in samples taken from his kidney was 4.6 mg/kg. The kidney concentration of mercury in the other case where this type of estimation was carried out was 34.2 mg/kg in a 20-year-old female who died as early as mid-January with a liver concentration of mercury of 6.6 mg/kg. The highest liver concentration of mercury (75.5 mg/kg) was found in a 13-year-old girl who died in hospital. A pregnant woman 25 years old had a level of 17.7 mg/kg in her liver, while that of her fetus contained 4.1 mg/kg. In the 3 cases where, in addition to total mercury, inorganic mercury was estimated, livers with 17.4, 17.7, and 22.4 mg/kg of total mercury had 5.5, 2.8, and 9.2 mg/kg of inorganic mercury; in these livers 16-40% of the mercury was in the inorganic form. The 40-year-old female whose clinical history was known had 16.5 mg/kg in her liver. Her blood concentration of mercury at the time of her death on 19 March was 4.02 µg/ml. The first blood estimation, made 13 days earlier, was slightly higher - 4.43 µg/ml. She was deaf and seriously ataxic at that time.

Table 2 shows the relationship between the liver concentration of mercury and the date of death.

DISCUSSION

The liver concentrations of mercury in the autopsy cases in Iraq and in those reported from the Minamata outbreak[3,4] reveal striking differences.

(a) The range of liver mercury concentrations

In the Minamata cases, at death the highest mercury concentration in the liver was 70.5 mg/kg; in the Iraq cases it was 75.5 mg/kg; the lowest level found in 2 Minamata patients, who died between 100 and 120 days after the onset of symptoms, was 22 mg/kg; the lowest liver concentration found in the 51 Iraqi victims was 1.4 mg/kg; 28 had less than 20 mg/kg, 13 less than 10 mg/kg, and 5 less than 5 mg/kg.

FIG. 1. POST-MORTEM DISTRIBUTION OF MERCURY CONCENTRATION IN THE LIVER OF 51 SUBJECTS SUSPECTED OF HAVING DIED FROM METHYLMERCURY POISONING

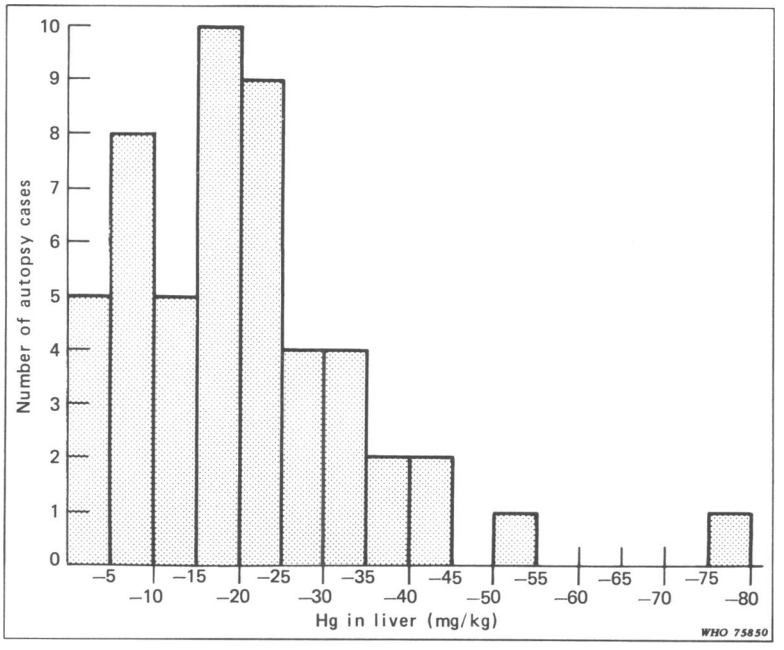

TABLE 2. LIVER CONCENTRATIONS OF MERCURY IN RELATION TO THE TIME OF DEATH

Hg concentration (mg/kg)	Time of death (1972)					
	8 Jan.- 21 Jan.	22 Jan.- 4 Feb.	5 Feb.- 28 Feb.	29 Feb.- 16 March	Unknown, but not later than Feb.	Total
- 10.0	4	1	5	-	3	13
10.1 - 20.0	2	-	9	2	2	15
20.1 - 30.0	2	1	6	-	4	13
30.1 -	-	1	6	-	3	10
Total	8	3	26	2	12	51

(b) The nature of exposure

The exposure to methylmercury in both outbreaks was oral, but in the Minamata outbreak fish contaminated by methylmercury might also have contained selenium, which is known to moderate the toxicity of methylmercury.[7] The consumption of bread made from methylmercury-treated wheat did not offer this possibility of a moderating effect. However, it must be pointed out that the same plotting technique, applied by a Swedish expert group to non-lethal cases of methylmercury poisoning from the Niigata outbreak,[4] gave considerably lower blood values in relation to the onset of the symptoms than the blood mercury concentrations measured in the Iraq outbreak.[8]

(c) Duration of exposure and length of illness before death

The exposure time in the Minamata outbreak was long-term, probably lasting for years. In Iraq, exposure was short; ingestion of bread contaminated with methylmercury took place for a period not exceeding approximately 2 months. In Iraq the first death occurred during this 2-month exposure period, which ended for the majority of people in the middle of January 1972 as a result of an intensive educational programme. In the 51 cases the maximum time between the end of exposure and death could not have been longer than 60 days, but, as Table 2 indicates, the majority died within 45 days after the presumed end of exposure. In the Minamata cases, 6 people died within 60 days and 6 people between 60 and 120 days after the onset of symptoms. However, the onset in these cases meant the onset of severe symptoms that enforced hospitalization, and not the occurrence of the first symptoms. Tokuomi[9] gives the following description of the type of onset in the Minamata cases: ". . . in most cases the onset was slow, but some cases occurred suddenly after drinking wine. Usually the first symptom was tingling and numbness in the tips of the extremities and in the perioral region"; thereafter the characteristic "signs and symptoms of methylmercury poisoning developed in 1-3 weeks". It seems very likely that during the slow progress before the occurrence of severe symptoms, people did not stop eating contaminated fish and the regression line drawn by the Swedish expert group[4] can indicate only the organ concentration of mercury at the time of hospital admission, which approximates to the onset of severe symptoms.

As a result of the difference in exposure time in Minamata and in Iraq, the progress of the disease in Minamata was slower, with longer periods between the onset of the first symptoms and severe symptoms and between the first symptoms and death than in Iraq. The difference in liver mercury concentrations between the Minamata and Iraq victims may have its origin in differences between exposure and the course of the disease. The 10-year-old boy with a liver mercury concentration of 1.4 mg/kg might have died from the acute gastrointestinal effect of methylmercury, which aggravated some pre-existing disease. However, it seems reasonable to suppose that, when as a result of an acute exposure to methylmercury the liver concentration is in the range of 10 mg/kg, methylmercury can result in death without any additional disease.

Observations on cases of methylmercury poisoning of occupational origin indicate that in acute cases the liver mercury concentration does not necessarily reach the level given by the Swedish expert group. A patient who died 53 days after exposure and approximately 10-15 days after the onset of symptoms had 19.6 mg/kg of mercury in his liver[10] and another, who died 30 days after the onset of symptoms, had 14.1 mg/kg in the liver and 4.0 μg/ml mercury in the blood, approximately the same values as the Iraqi case with known medical history. These 2 occupational cases of methylmercury poisoning, like the Iraq cases, do not fit into the regression line plotted by the Swedish expert group. Clearly any extrapolation of tissue mercury levels in relation to the toxic effects of methylmercury must take account of the duration and intensity of the preceding exposure.

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RESUME

DOSAGE DES COMPOSES MERCURIELS DANS DES SPECIMENS DE FOIE ET DE REIN PRELEVES A L'AUTOPSIE

Cinquante et un spécimens de foie prélevés à l'autopsie ont été analysés pour déterminer la concentration des composés mercuriels. Treize spécimens contenaient moins de 10 mg de mercure par kg, avec une valeur minimale de 1,4 mg/kg, ce qui indique que chez les cas suspects, le décès n'a pas toujours été dû à une exposition mortelle aux composés méthylmercuriels. Dans 28 foies la concentration des méthylmercuriels s'est échelonnée entre 10 et 30 mg/kg. Des dosages complémentaires, en nombre limité, ont montré que, dans une proportion de 71%, le mercure décelé dans le foie se présentait sous forme de composés organiques et que la concentration du mercure dans le foie d'un foetus de 7 mois ne représentait que 25% de la concentration dans le foie de la mère. Chez un malade décédé à l'hôpital avec une concentration de 4,1 µg/ml de mercure dans le sang, le foie contenait 16,5 mg de mercure par kg.

Les différences entre ces résultats et ceux des observations faites lors de l'épisode d'intoxication par méthylmercuriels au Japon sont analysées. Toute extrapolation concernant le rapport entre la concentration de mercure dans les tissus et les effets toxiques des méthylmercuriels doit tenir compte de l'intensité et de la durée de l'exposition.

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